

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

see form PCT/ISA220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/011287

International filing date (day/month/year)
08.10.2004

Priority date (day/month/year)
10.10.2003

International Patent Classification (IPC) or both national classification and IPC
A61L27/02, A61L27/04, C12N5/06

Applicant
WITTE, Frank

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA220.

3. For further details, see notes to Form PCT/ISA220.

Name and mailing address of the ISA:



European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Menidjel, R

Telephone No. +31 70 340-3680



**WRITTEN OPINION OF THE
 INTERNATIONAL SEARCHING AUTHORITY**

International application No.
 PCT/EP2004/011287

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

BEST AVAILABLE COPY

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/011287

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-13,15,16

because:

☒ the said international application, or the said claims Nos. 1-13,15,16 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. , 2, 4-13

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See separate sheet for further details

BEST AVAILABLE COPY

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/011287

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☒ paid additional fees under protest.
 - ☐ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☒ complied with
 - ☐ not complied with for the following reasons:
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 14,15

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-16
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-16
Industrial applicability (IA)	Yes: Claims	14
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

- The subject-matter of present claims 1-13,15,16 is related to a method for treatment of the human or animal body from surgery or therapy. Using its discretion, the present authority decided not to carry out an internal preliminary examination on that subject-matter (Article 34(4)(a) PCT in conjunction with Rule 67.1(iv) PCT).

For the assessment of the present claims 1-13,15,16 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

D1: US-A-4 954 349 (SHETH PRAVIN B ET AL) 4 September 1990 (1990-09-04)

D2: US-B1-6 211 143 (GIL GABRIEL ESPELLETA ET AL) 3 April 2001 (2001-04-03)

2. Novelty (Article 33(2) PCT)

- The subject-matter of present claims 1-16 is considered as novel over the cited prior art (Article 33(2) PCT) for the following reasons:

- None of the documents cited in the international search report refers to a **method for the generation of chondrons** comprising the step of cultivation of cells at **unphysiologically high extra cellular concentrations of magnesium**, characterized in that **at least once the unphysiologically high extra cellular Mg concentration is increased** during cell cultivation.

3. Inventive Step (Article 33(1),(3) PCT)

- Although novel, the subject-matter of present claims 1-16 is considered as not inventive for the following reasons (Article 33(1),(3) PCT):

- The subjective problem to be solved by the present application is to provide a method for the generation of chondrons and of cartilaginous tissue.

- The solution proposed in the present application is a method as described in present claim 1.

- Document D1, which is considered as the closest prior art, describes **a method of treating or preventing potassium and magnesium deficiency in skeletal and cardiac muscle by oral administration of magnesium salt.**

- The difference between the teaching of the closest prior art and the claimed subject-matter appears to be the unphysiologically high extra cellular concentrations of magnesium (Mg) characterized in that at least once the unphysiologically high extra cellular Mg concentration is increased during cell cultivation.

- Document D2 describes a method for increasing cartilaginous mass of joints in a mammal **by ingestion of a hydrolysed gelatin enriched with magnesium.**

- The person skilled in the art would regard it as a normal option to include the features described in document D1 in document D2 in order to solve the problem posed and therefore, to come to the claimed solution.

Therefore, the subject-matter of present claims 1-16 does not involve an inventive step (Article 33(1),(3) PCT).